

Objection to the Specification

The Brief Description of the Drawings stands objected to by the Examiner for referring to "Figure 1" rather than "Figures 1A-C." Applicants have amended the specification herein to make this correction. Accordingly, withdrawal of this objection is respectfully requested.

Double Patenting Rejection

Claims 422-441 stand provisionally rejected by the Examiner under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 444-465 of copending application Serial No. 09/565,427. Applicants will address this provisional rejection at such time as claims are otherwise indicated to be in condition for allowance.

Rejection Under 35 U.S.C. § 102

Claims 422, 427-431, 433-441 stand rejected by the Examiner under 35 U.S.C. § 102(e) as being anticipated by Van Gemen *et al.* (U.S. Patent No. 5,679,553). Applicants respectfully traverse this rejection for the reasons that follow.

Anticipation requires that all elements of a claim exist in one prior art source. *In re Marshall*, 198 USPQ 344 (CCPA 1978). Without a single prior art reference which discloses every element of the claimed invention, the claim is not anticipated under 35 USC § 102. Applicants submit that the reference cited by the Examiner in support of this rejection not only fails to anticipate the claimed invention of the subject application, it actually teaches away from the use of primers which include one or more 2'-O-methyl modifications.

Van Gemen is cited by the Examiner for disclosing kits for amplifying a target nucleic acid sequence contained in a target nucleic acid which comprises an oligonucleotide primer containing a first base region which forms a stable hybrid with a second base region contained in the target nucleic acid under amplification conditions, where the first base region contains one or more

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ribonucleotides modified to include a 2'-O-methyl substitution to the ribofuranosyl moiety. The Examiner submits that such kits would inherently include written instructions for their use. Various sections of Van Gemen are cited by the Examiner in an effort to support this rejection.

Applicants have carefully reviewed the sections of Van Gemen cited by the Examiner, and the patent as a whole, but have been unable to find any suggestion to modify primers to include 2'-O-methyl substitutions. Instead, the Van Gemen disclosure is directed to the use of detection and capture oligonucleotides modified to prevent their degradation by a nuclease in a sample *following amplification*. See, e.g., Van Gemen at column 5, lines 6-11 and 59-61. In fact, Van Gemen teaches that his invention includes subjecting a detection oligonucleotide:amplified product hybridization complex to a degradative treatment "under circumstances such that at least part of the hybridisation complex capable of hybridizing to the primer is degraded." See Van Gemen at column 4, lines 45-61 (emphasis added). Thus, rather than protecting priming sites on amplified product by including 2'-O-methyl modified primers, it is actually Van Gemen's objective to degrade these regions following amplification.

For the reasons presented, Applicants submit that the claims are fully patentable in view of Van Gemen. Accordingly, withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C. § 103

Claims 423-426 stand rejected by the Examiner under 35 U.S.C. § 103(a) as being unpatentable over Van Gemen *et al.* (U.S. Patent No. 5,679,552). Applicants respectfully traverse this rejection for the reasons that follow.

Van Gemen is cited by the Examiner for disclosing kits containing oligonucleotide primers containing one or more ribonucleotides modified to include a 2'-O-methyl substitution to the ribofuranosyl moiety and for inherently containing written instructions for their use. The claims

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under consideration are directed to oligonucleotide primers which contain clusters of at least 4, at least 6 or at least 8 2'-O-methyl modified ribonucleotides or where all of the nucleotides are ribonucleotides modified to include a 2'-O-methyl substitution to the ribofuranosyl moiety. Since Van Gemen fails to disclose or suggest 2'-O-methyl modified primers, the introduction of additional limitations into these claims distances them even further from the teachings of Van Gemen. Moreover, the basis for this rejection rests solely on the Examiner's unsupported conclusion that the motivation for these particular limitations would have been routine optimization. If this rejection is to be maintained, then Applicants submit that the Examiner needs to present (i) evidence that 2'-O-methyl modified primers are suggested by the prior art and (ii) support for why those skilled in the art would have been motivated to make the *specifically claimed modifications*, without relying on the benefit of hindsight. See MPEP § 2141.01, Section III, at 2100-91 (Rev. 1, February 2000).

Claim 432 stands rejected by the Examiner under 35 U.S.C. § 103(a) as being unpatentable over Van Gemen *et al.* (U.S. Patent No. 5,679,553) in view of Cruickshank (U.S. Patent No. 5,091,519). Applicants respectfully traverse this rejection for the reasons that follow.

Van Gemen is cited by the Examiner for disclosing kits containing oligonucleotide primers containing one or more ribonucleotides modified to include a 2'-O-methyl substitution to the ribofuranosyl moiety and for inherently containing written instructions for their use. Cruickshank is cited for disclosing the use of acridinium esters as chemiluminescent labels to detect nucleic acid hybridization. As discussed above, Van Gemen does not disclose or suggest 2'-O-methyl modified primers and Cruickshank has not been relied upon for satisfying this deficiency. Accordingly, Applicants submit that a *prima facie* case of obviousness has not been presented.

For the reasons presented, Applicants submit that the claims are fully patentable in view of the cited references, when considered alone or in combination. Accordingly, withdrawal of this rejection is respectfully requested.

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Marked-Up Copy of Amendment

In accordance with 37 C.F.R. § 1.121, Applicants are attaching hereto a marked-up version of the amendment made to the specification herein.

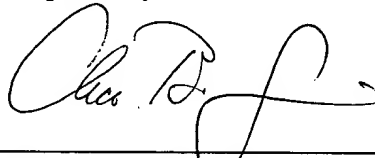
Applicants submit that the subject application is in condition for allowance and Notice to that effect is respectfully requested.

No fee is believed due in connection with this Amendment. If Applicants are mistaken, please charge the amount due to Deposit Account 07-0835.

Certificate of Mailing

I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is being deposited on the date indicated below with the U.S. Postal Service as First Class Mail Commissioner for Patents, Washington, D.C. 20231.

Respectfully submitted,



Date: April 2, 2001

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Marked-Up Copy of Amendment to Specification

1. The following is a marked-up version of the amendment made to the specification at page 10, lines 14-15:

[Figure] Figures 1A-C [provides] provide the IUPAC nomenclature for a sampling of acridinium esters that may be used as detectable chemiluminescent labels in the present disclosure.